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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,985	11/28/2000	Philip Michael Savage	674544-2001	8380
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FROMMER LAWRENCE & HAUG 745 FIFTH AVENUE- 10TH FL. NEW YORK, NY 10151			EXAMINER VANDERVEGT, FRANCOIS P	
			ART UNIT 1644	PAPER NUMBER

DATE MAILED: 06/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/724,985

Applicant(s)

SAVAGE, PHILIP MICHAEL

Examiner

F. Pierre VanderVegt

Art Unit

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 February 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,4,6-9 and 11-75 is/are pending in the application.
- 4a) Of the above claim(s) See Continuation Sheet is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,4,6-9, 11-14,16-18,26,27,29,32,33,37,46-53,56,57,60,63,64,67-70 and 75 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 01272004.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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Continuation of Disposition of Claims: Claims withdrawn from consideration are 15,19-25,28,30,31,34-36,38-45,54,55,58,59,61,62,65,66 and 71-74.

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DETAILED ACTION

This application is a continuation-in-part of Application Serial Number PCT/GB99/01764.

Claims 2, 5, 10 have been canceled.

New claims 30-75 have been added.

Claims 1, 3, 4, 6-9 and 11-75 are currently pending.

Claims 19-22 and 25 stand withdrawn as being drawn to a non-elected invention.

Request for Interview

1. Applicant has requested that an interview with the Examiner and a Supervisory Examiner be held in the event that the response filed February 28, 2005 resulted in any Office Action being issued other than a Notice of Allowability.

However, in view of the NEW GROUNDS of rejection presented below, Applicant is being given an opportunity to review the new rejection prior to said interview being held. Accordingly, Applicant is invited to schedule said interview after having an opportunity to review the ground of rejection newly presented.

Election/Restrictions

2. Applicant's election with traverse of the species tumor cells, malignant cells or leukemia cells in the reply filed on January 22, 2004 is acknowledged. The traversal is on the ground(s) that there a disclosed relationship between the species because they all constitute target cells that can be bound by the complex of the claimed invention. This is not found persuasive because each of the different species is identified by a different type of cell from a unique source, requiring a separate search of the antigenic peptides derived from the cell type and the surface antigens to which the complex may bind.

3. The species requirement had previously been withdrawn. However, in view of the recent identification of art perceived to read upon the elected species **the species requirement is hereby reinstated** for the reasons set forth in the Office Action mailed August 27, 2004 and reproduced supra.

4. **Claims 15, 23, 24, 28, 30, 31, 34-36, 38-45, 54, 55, 58, 59, 61, 62, 65, 66 and 71-74 are withdrawn** from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on January 22, 2004.

5. **Claims 19-22 and 25 stand withdrawn** as being drawn to a non-elected invention.

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6. Accordingly, claims 1, 3, 4, 6-9, 11-14, 16-18, 26, 27, 29, 32, 33, 37, 46-53, 56, 57, 60, 63, 64, 67-70 and 75 are the subject of examination in the present Office Action.

In view of Applicant's amendment and remarks filed February 28, 2005, only the following ground of rejection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 3, 4, 6, 9, 11-18, 23, 24, 25-39, 46-49, 52-75 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection.

It was previously stated: "The claims are drawn to a complex comprising a complex comprising an MHC class I molecule joined to a linking polypeptide specific for a target cell, wherein the MHC class I molecule and the linking peptide are joined to one another via a coupling system comprising a first small molecule and a second small molecule.

The scope of the claims, drawn to a complex[] where the coupling system comprises "small molecules" to the immunogen, includes in scope a number of embodiments for which there is no sufficient written description in the specification. The term "small molecule" is a broad term encompassing a plethora of organic and non-organic molecules and is not defined in the instant specification in such a manner as to apprise the artisan of the scope of small molecules encompassed by the claims or that Applicant had possession of a representative number of species of "small molecules." The specification is limited in its description of small molecules, reciting only, "The coupling system may comprise a two- or three-step chain of well-characterised paired small molecules, joined to the antibody and the HLA class I molecule so as to form a stable bridge between the two. Examples of paired small molecules which might be used in this connection include (but are not limited to) biotin and avidin/streptavidin [...] and calmodulin and calmodulin binding peptides [...]" at lines 1-8 of page 7, for example. *Vas-Cath Inc. v. Mahurkar* ((CAFC, 1991) 19 USPQ2d 1111), clearly states that "Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See *Vas-Cath* at page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). It is respectfully submitted that the instant specification does not describe a sufficient number of species to provide full descriptive support of the genus encompassing all such molecular adjuvants.

Therefore only the disclosed species of "small molecules," namely the paired small molecules

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biotin - avidin/streptavidin and calmodulin - calmodulin binding peptides, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see *Vas-Cath* at page 1115)."

Applicant's arguments filed February 28, 2005 have been fully considered but they are not persuasive.

Applicant asserts that the specification provides sufficient guidance for the artisan to select additional small paired molecules beyond those actually disclosed because the artisan would recognize that small paired molecules such as leucine zippers or barnstar and barnase would function similarly to the disclosed paired small molecules biotin - avidin/streptavidin and calmodulin - calmodulin binding peptides. In the present case, the genus of small molecules is perceived to be quite large, however Applicant has named only two paired members of the genus in the specification. While biotin is unquestionably a small molecule, avidin is a four subunit 66KDa complex of 128 amino acid peptide molecules, calmodulin is a 15-19Kda protein and the identity of the "calmodulin binding protein" has not been established, so its size is not known. Avidin and calmodulin are not what one skilled in the art would readily identify with the term "small molecule." Inclusion of a 66Kda protein complex as the definition of a "small molecule" descriptive of the genus encompasses a great number of species. Further, Applicant has not described any structural features of biotin - avidin/streptavidin or calmodulin - calmodulin binding peptides that are in common with any other small molecules, paired or otherwise. Applicant's position basically reduces down to the position that naming biotin - avidin/streptavidin and calmodulin - calmodulin binding peptides as paired small molecules renders the use of all other small molecules obvious to the artisan. Applicant is reminded that obviousness is not the standard for descriptive support. Entitlement to a filing date does not extend to subject matter that is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977). Furthermore, the term "small molecule" in the claim reads upon small molecules that are not composed of amino acid residues and such small molecules are not described in the specification. Neither does the specification set forth any description of what is considered a "small molecule," even in terms of the peptides encompassed. The term "small" is a relative term and does not connote any size on its own. While the claims are read in light of the specification, limitations from the specification are not read into the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 29 and 75 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 29 and 75 are indefinite in reciting a pharmaceutical pack or kit containing one or more pharmaceutical compositions claimed in a base claim. In each case, the base claim is drawn to a single pharmaceutical composition and therefore does not provide adequate antecedent basis for reciting “one or more” of the “compositions.”

Applicant has amended the claims by striking the recitation of “of the” from the claims. Applicant asserts that this amendment overcomes the rejection because “said compositions” lack antecedent basis because a singular “composition” is recited in base claims 26 and 69.

The following NEW GROUNDS of rejection were not necessitated by Applicant’s amendment. Accordingly, this Office Action is made NON-FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 6-8, 12 and 56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6, 7, and 8 each recite the limitation “comprises a three-step chain of small molecules” in the claim. There is no antecedent basis for this limitation in the claim. The claims recite only a “first small molecule joined to the linking polypeptide” and a “second small molecule joined to the HLA class I molecule.” There is no basis in the claims for a third small molecule and it is not clear how the third is functionally related to the first and second.

The terms “strong” and “powerful” in claims 12 and 56 are relative terms that render the claim indefinite. The terms are not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of

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the scope of the invention. The metes and bounds of the terms have not been established in the claim or the specification.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

11. Claims 1, 3, 4, 9, 11-14, 16-18, 26, 27, 29, 32, 33, 37, 46-50, 52, 53, 56, 57, 60, 63, 64, 67-70 and 75 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,548,067 B1 to Seeman et al (filing date June 2, 1995; A on form PTO-892).

The '067 patent teaches a complex comprising an HLA class I molecule comprising a T cell binding portion and an attaching means for selectively attaching said HLA class I molecule to a target cell. The attachment means comprises a linking polypeptide with specific affinity for a molecule on the surface of the target cell, wherein the linking polypeptide is an antibody molecule that binds to an antigen on the target cell or a molecule that binds to a receptor on the cell (Figure 34, column 3, lines 11-24 and 49-62 in particular). The '067 patent teaches the binding of a recognition peptide (allodeterminant) to the HLA class I molecule (Fig. 1, column 1, lines 58-62 and column 9, lines 40-44 in particular). The '067 patent further teaches that the HLA class I molecule and the linking polypeptide of the complex are directly covalently linked to one another or that the complex comprises a coupling system forming a stable bridge between the HLA class I molecule and the linking polypeptide comprising the small molecules biotin and avidin (Abstract, Figure 34, column 3, lines 11-17 and column 4, lines 5-13 in particular). the '067 patent further teaches that the allotype of the HLA class I molecule of the complex

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may be different from the HLA class I haplotype of a subject the complex is administered to (column 3, line 38 to column 4, line 4 in particular). The prior art teaching anticipates the claimed invention.

Claims 29 and 75 are drawn to a pharmaceutical pack or kit and are included in this ground of rejection. The kit recited in the claims comprises three components, the claimed complex, wherein the complex is in one or more containers and written instructions for administering the complex to a patient. In regard to the containers, while the '063 does not explicitly recite the presence of a container, it would be readily appreciated by the artisan that the complex as taught by the '063 patent would have been held in a container. Accordingly, the '063 patent demonstrates possession of 2 of the 3 elements of the kit. However, the printed matter on the instructions does not lend patentable weight as a limitation of the claimed invention because the recited intended use does not physically or chemically change the nature of the agent within the container and the artisan can still use the agent for other purposes. The intended use of a product, in this case an HLA class I/attachment means complex, does not materially change the product as the product can still be used for other purposes, such as identifying and/or immobilizing target cells in vitro. The recited "limitations" only further limit the intended use method printed on the instructions and do not change the physical and/or chemical properties of the components of the kit. In *In re Haller* (73 USPQ 403 (CCPA 1947)) the Court decided upon a case in which "it is not alleged by the Examiner or the board that the use of the involved compound as an insecticide is old or obvious and, in fact a claim covering broadly a process comprising the application of that compound to insects for the purpose of destroying them, has been allowed. In the instant case the appealed claim calls for a packaged product of an old compound labeled to indicate that the compound is intended for use as an insecticide." It is respectfully submitted that the facts of *In re Haller* are directly pertinent to the instant case. Applicant relies, as in *In re Haller*, upon printed matter reciting an intended use of the otherwise old compounds and compositions. The Court noted in *In re Haller* that "It is well settled that the application of particular printed matter to an old article cannot render the article patentable" and decided that, "the mere labeling of an old composition as an insecticide does not make it a new or different composition within the meaning of the patent statutes" and "Whether the statement of intended use appears merely in the claim or in a label on the product is immaterial so far as the question of patentability is concerned" in affirming the rejection. In *In re Venezia* (189 USPQ 149 (CCPA 1976)) the Court decided that the kit components were limited by the instructions listed in the claims because said kit components had to be adapted in a particular manner in order to meet the final assembly instructions that were part of the claim. The Court stated however that, "what may or may not happen in the future is not a part of the claimed invention" (emphasis by Court). The Court decided that the instructions of the claim were material to the claim

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because, "Rather than being a mere direction of activities to take place in the future, this language imparts a structural limitation to the sleeve" (emphasis added). The court reasoned this position by stating, "this language also defines present structures or attributes of the part of the 'kit' identified as the housing, which limits the structure of the housing to those configurations which allow for the completed connector assembly desired." It is respectfully submitted that, in the instant case, the instructions do not modify the complex comprised in the claimed kit, i.e., the complex does not have to be altered for use commensurate with the instructions, rather the printed instructions merely set forth steps for what may be done with the kit components in the future. Accordingly, the printed instructions do not lend patentable weight to the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 3, 4, 9, 11-14, 16-18, 26, 27, 29, 32, 33, 37, 46-49, 51-53, 56, 57, 60, 63, 64, 67-70 and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,548,067 B1 to Seeman et al (filing date June 2, 1995; A on form PTO-892) in view of Neri et al (J. Invest. Dermatol. [1996] 107(2):164-170; U on form PTO-892).

The '067 patent has been discussed supra.

The '067 patent does not teach the use of calmodulin and calmodulin binding protein as paired small molecules for joining the HLA class I molecule of the complex to the attaching means of the complex.

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Neri teaches a method and a compound for attaching an anti-tumor molecule to another active compound by recombinant production of a single chain version of the antibody with a calmodulin peptide attached to the C-terminus (see entire document). Neri teaches that therapeutic peptides can be attached to the antibody by attaching them to a high-affinity calmodulin ligand, such as calmodulin binding protein. It is noted that the 225.28S antibody taught by Neri is the same as one of the anti-tumor antibodies exemplified in the instant specification as a preferred embodiment of an attachment means.

It would have been prima facie obvious to a person having ordinary skill in the art at the time the invention was made to replace the biotin - avidin/streptavidin taught by the '063 patent with the calmodulin - calmodulin binding protein taught by Neri. The artisan would have been motivated to make the substitution by the teaching of Neri that calmodulin is poorly immunogenic and can be targeted with chemically modified high-affinity calmodulin ligands (Abstract in particular). the artisan would have had a reasonable expectation of success based upon the teaching of Neri that calmodulin did not interfere with binding of antibody to target cells and that such an antibody construct is useful as a building block for therapeutic applications.

The following NEW GROUNDS of objection and rejection have been necessitated by Applicant's amendment.

Claim Objections

13. Applicant is advised that should claim 4 be found allowable, claim 49 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 4 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 4 and 49 are ambiguous and unclear in that they do not state how HLA and the "attaching means are structurally related. The claim recites only that they are parts of a "complex." Are the HLA class I molecule and the attaching means joined? If so, by what?

Claims 4 and 49 each recite the limitation "said linking polypeptide" in line 7 of the claim. There is no antecedent basis for this limitation in the claim. The independent claim makes no earlier recitation of a "linking polypeptide."

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D. *PV*
Patent Examiner
June 7, 2005

David A. Saunders
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PRIMARY EXAMINER
ART UNIT ~~182~~-1644